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Decomposition Products of Inactive

Dihydroaminocampholytic Acid

Chemistry

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DECOMPOSITION PRODUCTS OF INACTIVE  
DIHYDROAMINOCAMPHOLYTIC ACID

BY

PAUL STANLEY WOODWARD  
B. S. Stetson University, 1908

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THESIS

Submitted in Partial Fulfillment of the Requirements for the

Degree of

MASTER OF SCIENCE

IN CHEMISTRY

IN

THE GRADUATE SCHOOL

OF THE

UNIVERSITY OF ILLINOIS

1913



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UNIVERSITY OF ILLINOIS  
THE GRADUATE SCHOOL

May 29th,

19613

I HEREBY RECOMMEND THAT THE THESIS PREPARED UNDER MY SUPERVISION BY

PAUL STANLEY WOODWARD

ENTITLED DECOMPOSITION PRODUCTS of INACTIVE

DIHYDROAMINOCAMPIC ACID.

BE ACCEPTED AS FULFILLING THIS PART OF THE REQUIREMENTS FOR THE

DEGREE OF ~~Master of Science.~~

*W. A. Noyes*

In Charge of Major Work

*W. A. Noyes*

Head of Department

Recommendation concurred in:

\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

}

Committee

on

Final Examination


247476







DECOMPOSITION PRODUCTS of INACTIVE  
DIHYDROAMINOCAMPHOLYTIC ACID



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The present work was undertaken in September 1912 at the suggestion of Professor W. A. Noyes, and has been carried out in the Chemical Laboratory of the University of Illinois under his supervision during the academic year of 1912-13

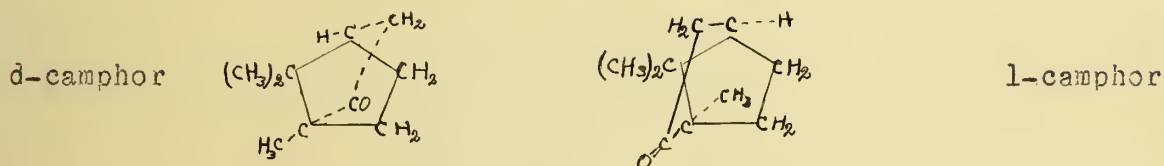
I wish to express my sincere gratitude to Professor Noyes for his sympathetic assistance and untiring patience during the progress of this work.





# DECOMPOSITION PRODUCTS of INACTIVE DIHYDROAMINOCAMPHOLYTIC ACID.

Inactive or synthetic camphor is really a mixture of the dl-camphor, so for our formula we must go back to the active camphor structure. The structural formula suggested by Bredt<sup>1</sup> in 1893 has been generally accepted, and so for the two, the d and the l camphors we have the following : -



As the d-camphor has a positive rotation and the l-camphor a negative, a mixture of equal parts would give the racemic or inactive camphor.<sup>2</sup>

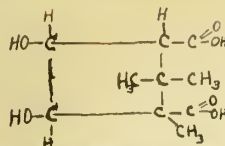
Each camphor, if oxidised with nitric acid will give an acid called camphoric acid. These melt at 187° and the d-camphoric acid has a rotation of  $(\alpha)_D = +49.7^\circ$ <sup>3</sup> while the l-camphor <sup>is acid</sup> has a negative rotation of the same amount.

Komppa<sup>4</sup>, after he had succeeded with the synthesis of apocamphoric acid ( which is an oxidation product of camphene); tried to methylate the diketoapocamphoric acid to obtain the diketo-camphoric ester. This was accomplished by the use of sodium and

- 
1. Ber. 26 3049 (1893)
  2. Armstrong & Tilden. Ber. 12 1756 (1879 )
  3. Laurent. Ann. 22 138 also Noyes. Am.Chem.J. 16 501 (1894)
  4. Komppa; Ber 36 4332 also Perkin & Thorpe

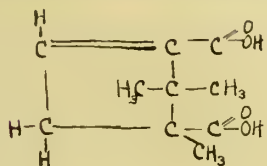


iodine in absolute alcohol. This can be converted into the dihydroxycamphoric acid:-

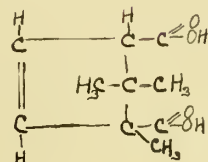


by soda solution, with sodium amalgam in a stream of carbon dioxide.

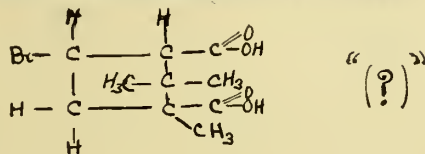
The racemic dehydro camphoric acid:-



OR



was obtained by heating the dihydroxy acid with hydrobromic acid and a little amorphous phosphorus. By heating for some time at 125° with hydrobromic and glacial acetic acids the dehydrated camphoric acid was converted into the  $\beta$  bromcamphoric acid

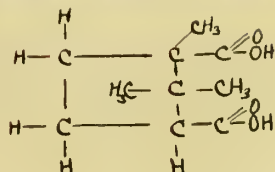


The  $\beta$  acid was not purified but was reduced with zinc dust and acetic acid, and the product was treated with acetyl chloride. The camphoric anhydride was extracted with ether and the product melted at 217° + 219°. This synthetic anhydride was compared with the natural product and found to be entirely identical. The racemic camphoric acid was recovered from the synthetic anhydride and when crystallised from dilute alcohol it formed small pointed prisms similar to the natural product, with a melting point of 200° - 202°.



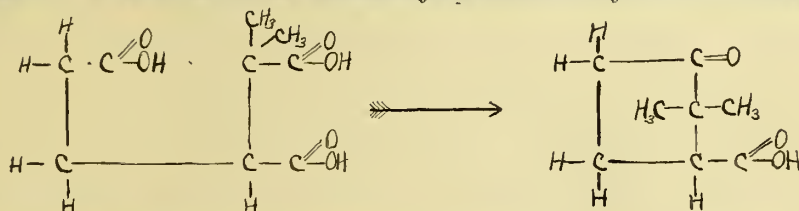


Komppa's Synthesis<sup>1</sup> established the structure of camphoric acid as: -

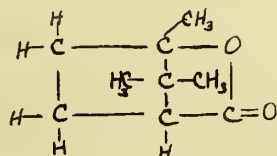


and this gives us the dl-camphoric acid. As this molecule contains a secondary and a tertiary carboxyl, it gives us two distinct series of compounds which depend only upon which carboxyl is attacked.

Using Perkin's Synthesis, the neutral sodium salt of  $\alpha\alpha$ -dimethylbutane $\alpha\beta\delta$ -tricarboxylic acid was heated with acetic anhydride at 140°, which gave 1-ketone-2,2-dimethylpentamethylene-3-carboxylic acid



The ethyl ester of this acid reacts readily with an ethereal solution of magnesium methyl iodide and gives us an  $\alpha$ -campholactone



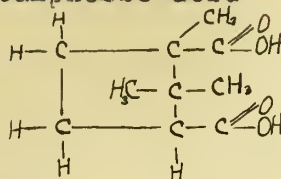
a substance which is of considerable interest on account of its close relationship to campholactone. The  $\alpha$ -campholactone dissolves in fuming hydrobromic acid and gives the  $\gamma$ -bromotrimethylpentamethylene-carboxylic acid. This easily loses hydrobromic acid and gives

$\alpha$ -campholytic acid.



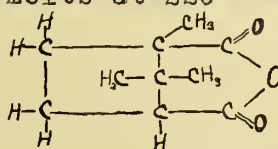


It was now a question of replacing the bromine atom in the bromotrimethylpentamethylenecarboxylic acid by the carboxyl group and thereby forming the camphoric acid



But considerable difficulty was here encountered because of the ease with which the compound decomposed. Finally, however, by the treatment of potassium cyanide and hydrocyanic acid, a small quantity of an oily acid was obtained. This was crystallised and the melting point found to be between  $180^\circ$  and  $190^\circ$ . This when treated with acetic anhydride showed a melting point of  $215^\circ - 217^\circ$ . When this was hydrolysed it gave an acid melting at  $204^\circ$  which characterised it as dl-camphoric acid.

Camphoric acid with acetyl chloride and acetic anhydride forms camphoric anhydride which melts at  $220^\circ - 221^\circ$  <sup>1</sup>



Camphoric anhydride when treated with strong ammonia, in alcoholic solution gives the <sup>camphoric</sup>ammonia salt of amidic acid, which on heating gives camphoric imide.

This by decomposition with sodium hydroxide would give the  $\alpha$  and  $\beta$  camphoramidic acids <sup>2</sup>.

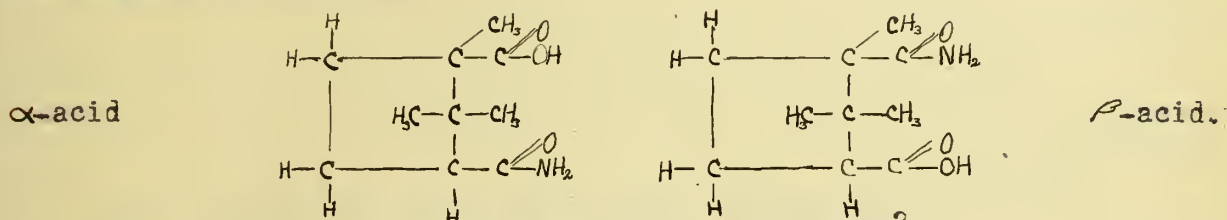
- 
1. Am.Chem.J. 16 502 (1894)  
 2. Am.Chem.J. 16, 508 (1894)





Noyes and Taveau<sup>1</sup> prepared the camphoramidic acid as follows.

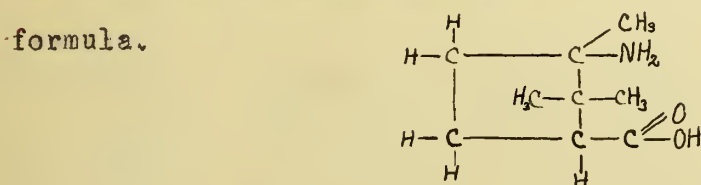
Camphoric anhydride was shaken with excess of strong ammonia in a pressure flask till the anhydride went into solution. On cooling rapidly, the ammonium salt of the  $\alpha$ -camphoramidic acid separated off. The  $\beta$ -camphoramidic sodium salt is precipitated by the addition of sodium hydroxide to the filtrate. The free amidic acids are obtained by dissolving their respective salts in warm water, cooling and precipitating with hydrochloric acid. This gives us our two series of compounds known as  $\alpha$  and  $\beta$  camphoramidic acids, which have the following structures.



The  $\alpha$ -acid was prepared by Auwers & Schnell.<sup>2</sup>

Claissen<sup>3</sup> obtained the same by heating isonitroso-camphor with fuming hydrochloric acid.

The  $\beta$ -camphoramidic acid by treatment with sodium hypobromite is converted into the dihydro-amino-campholytic acid, the chloride of which can be isolated and purified.<sup>4</sup> It has the following structural formula.



1. Am. Chem. J. 32, 287

2. Ber. 26, 1522.

3. Ann. 274, 81

4. Noyes. Am. Chem. J. 16, 310 & 503. also 24, 290



d-Dihydro-amino-campholytic acid when treated with nitrous acid yields four decomposition products<sup>1</sup> viz. : -

An unsaturated hydrocarbon ( Isolaurene ) boiling at 108°

An unsaturated acid ( $\alpha$ -Campholytic acid) boiling at 240-242°<sup>2</sup>

A lactone (Campholactone) melting at 115-116°

An hydroxy acid (Dihydrohydroxycampholytic acid) melting at 132°

### UNSATURATED HYDROCARBONS.

There are two hydrocarbons with the empirical formula  $C_{14}H_{24}$  viz.:- Isolaurene and Laurene and each is derived from camphor.

Blanc<sup>3</sup> synthesised Isolaurene and it has also been prepared from dihydroaminocampholytic acid<sup>4</sup>, from  $\beta$ -campholytic acid<sup>5</sup>, from sulphocamphylic acid<sup>6</sup>, from dihydrohydroxy campholytic acid<sup>4</sup> and by distilling copper camphorate<sup>7</sup>.

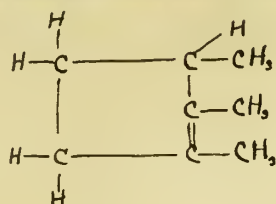
Laurene has been obtained by the slow distillation of camphanic acid<sup>8</sup> either alone or in a current of carbon dioxide; by the decomposition of the hydrochloride of aminolaurenic acid by nitrous acid<sup>9</sup>;

- 
1. Noyes; Am.Chem.J. 16, 307 & 505 also 17, 421. also Tiemann; Ber. 33, 2936 also Bredt; Ann. 314, 392.
  2. Walker; J. Chem. Soc. 63, 498.
  3. Blanc; Bull.Soc.Chim. (3) 19, 703 also Compt.Rend. 142, 1084.
  4. Prof. Noyes; Unpublished.
  5. Blanc; Bull.Soc.Chim. (3) 19, 703. Crossley&Renouf; J.Chem.Soc. 89, 29
  6. Damsky; Ber. 20, 2957
  7. Moitessier. Jahresb. (1866) 410
  8. Werden. Ann. 163 336 also
  8. Crossley&Renouf. J.Chem.Soc. 89, 27 & Aschan. Ann. 290 185
  9. Noyes. Am. Chem. J. 17, 432.





by the decomposition of the nitroso-derivative of aminolauronic anhydride with sodium hydroxide<sup>1</sup>; and by distilling calcium camphanate<sup>2</sup>. The structure may be represented as follows: -



### UNSATURATED ACIDS.

Synthetic camphor gives an inactive  $\alpha$ -campholytic acid which is converted into  $\beta$ -campholytic acid<sup>3</sup> with dilute mineral acids. Noyes and Knight<sup>4</sup> obtained a d-campholytic acid by the decomposition of isodihydroaminocampholytic acid by nitrous acid. The decomposition of the  $\alpha$ campholytic hydrobromide with sodium hydroxide gives a dl-campholytic acid<sup>5</sup>. The melting point of this acid is given in the literature as being 31° but the work herewith presented has raised it to 36°

By the reduction of the hydroiodide of dl-campholytic acid Noyes and Blanchard obtained a dihydrocampholytic acid<sup>6</sup>. From its bromine derivative, by treatment with alcoholic potash, a new campholytic acid was obtained which is not converted into  $\beta$ -campholytic acid by the

- 
1. Noyes; Am. Chem. J. 16, 508. also 32, 288.
  2. Rupe & Maull; Ber. 26, 1202.
  3. Noyes & Patterson; Am. Chem. J. 27, 432.
  4. J. Am. Chem. Soc. 32, 1672.
  5. Noyes & Blanchard; Am. Chem. J. 26, 289
  6. Am. Chem. J. 26, 289



action of dilute mineral acid. Its melting point is 90-91°.

Walker prepared an  $\alpha$ -campholytic acid by the electrolysis of the sodium salt of the  $\alpha$ -ethylester of camphoric acid<sup>1</sup>.

The same  $\alpha$ -campholytic acid was prepared by Prof. Noyes<sup>2</sup> by the decomposition of dihydroaminocampholytic acid with nitrous acid.

Perkins and Thorpe<sup>3</sup> have synthesised  $\alpha$ -campholytic acid.

This acid is a liquid boiling at 240 - 243° and can be reduced to dihydrocampholytic acid<sup>4</sup>. By distillation it gives campholytolactone<sup>5</sup> and with dilute mineral acid it is converted into the  $\beta$ -campholytic acid.

Artificial camphor yields dl-bromcamphoric anhydride and with sodium carbonate this gives dl-launonic acid and dl-camphanic acid. The latter on distillation forms more dl-launonic acid<sup>6</sup> which melts at 5 - 8°.

The decomposition of the nitroso derivative of aminocamphanic anhydride gave another unsaturated acid. This was obtained by Prof. Noyes and Taveau. Its melting point is from 152 - 154°<sup>7</sup>.

- 
1. J. Chem. Soc. 63, 498.
  2. Am. Chem. J. 16, 307 & 505
  3. J. Chem. Soc. 85, 128.
  4. Burke's Thesis.
  5. Blanc; Bull. Soc. Chim. (3) 25, 81.
  6. Noyes & Burke; J. Am. Chem. Soc. 34, 181.
  7. Am. Chem. J. 35, 383.





## HYDROXY ACIDS.

Prof. Noyes<sup>1</sup> obtained as one of the decomposition products of dihydroaminocampholytic acid with nitrous acid, a <sup>dihydro</sup> dihydroxycampholytic acid, melting at 132 - 133°. On distillation it gives isolaurolene.

Campholytolactone when boiled with alkalis, gives campholytolyic acid melting at 121°. It forms isocampholytic acid with dilute sulphuric acid<sup>2</sup>.

Campholactone on treatment with barium hydroxide gives an acid melting at 144 - 145°<sup>3</sup>. Dilute mineral acids easily decompose this<sup>4</sup>.

The ethyl ester of aminocamphonic acid when decomposed with sodium nitrite, yields hydroxylauronic acid<sup>5</sup>. There is some question as to whether or not this is a mixture.

The racemic form<sup>6</sup> of campholytic acid has been prepared by treating  $\rho$ -campholytic acid with hydrobromic acid and then with sodium hydroxide. We have prepared it from the inactive camphoric anhydride going through the inactive  $\rho$ -camphoramidic acid and the inactive dihydroaminocampholytic acid and then decomposing with sodium nitrite.

Prof. Noyes and Knight prepared the levo-isomer of dihydrohydroxycampholytic acid from isodihydroaminocampholytic acid<sup>7</sup>. This melts at 132° and has a negative rotation.

- 
1. Noyes; Am. Chem. J. 17, 424.
  2. Tiemann; Ber. 33, 2929.
  3. Tiemann; Ber. 33, 2946.
  4. Noyes & Burke; J. Am. Chem. Soc. 34, 182
  5. Noyes & Homberger; J. Am. Chem. Soc. 31, 279.
  6. Noyes & Blanchard; Am. Chem. Soc. 26, 286 and 27, 432.
  7. Noyes & Knight; J. Am. Chem. Soc. 32, 1672.





Cis-campholytic acid is prepared from cis-camphonololactone<sup>1</sup> by the action of barium hydroxide<sup>2</sup>. When heated to 255° it gives the lactone.

#### LACTONES.

Inactive  $\alpha$ -campholactone was prepared by Perkin and Thorpe<sup>3</sup> from ethyl-ketodimethylpentamethylenecarboxylate and magnesium methyl iodide. It distills at 155-157° under 50mm. pressure. It gives a hydroxy acid with the same structure as inactive  $\alpha$ -campholytic acid, because dilute mineral acids convert both into  $\beta$ -campholytic acid.

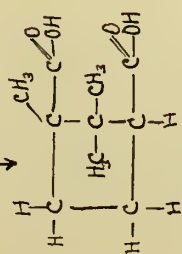
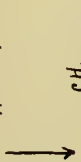
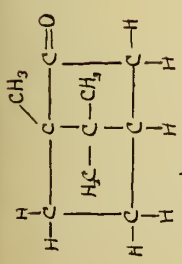
A lactone was derived from the dihydrohydroxycampholytic acid. It melts at 115° and has a positive rotation of 121.9°<sup>4</sup>

The decomposition of the hydrochloride of isodihydroaminocampholytic acid by sodium nitrite gives a lactone which has not yet been analysed<sup>5</sup>.

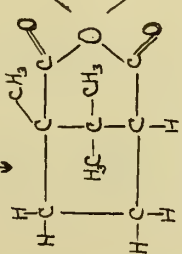
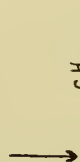
- 
1. Tiemann; Ber. 33, 2929.
  2. Noyes & Potter; J. Am. Chem. Soc. 34, 62.
  3. J. Chem. Soc. 85, 132.
  4. Innaugural Dissertation from the Laboratory of Prof. Bredt.
  5. Noyes & Knight; J. Am. Chem. Soc. 32, 1672.



Camphor

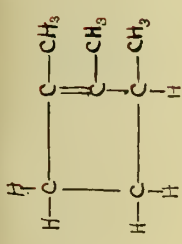


Camphoric Acid

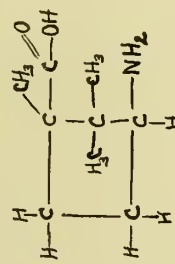


Camphoric Anhydride

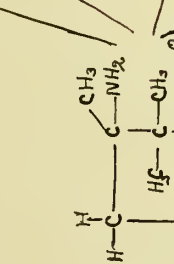
Lauroleone



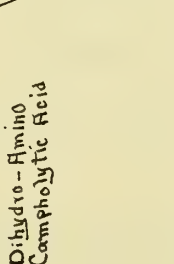
α-Camphoramidic Acid



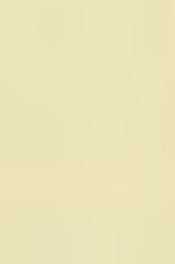
Amino-Camphoramic Acid



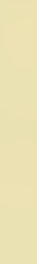
Dihydro-Amino Campholytic Acid



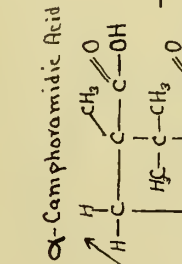
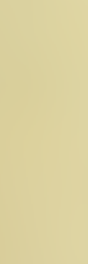
Campholyto Lactone



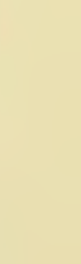
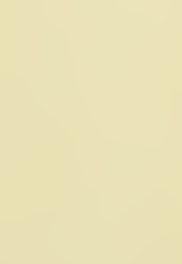
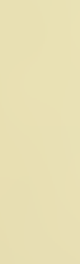
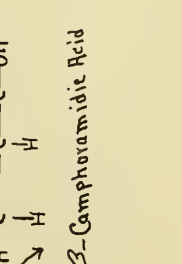
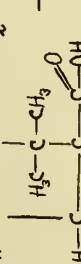
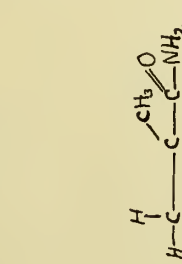
Iso-Lauroleone



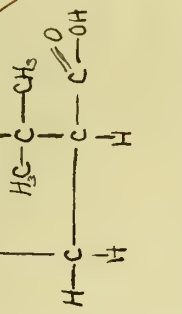
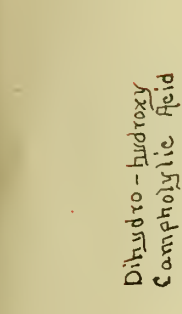
α-Camphoramidic Acid



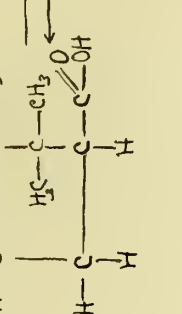
β-Camphoramidic Acid



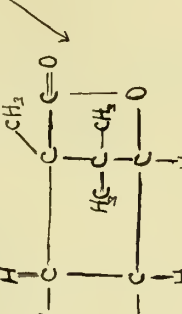
Dihydro-Hydroxy Campholytic Acid



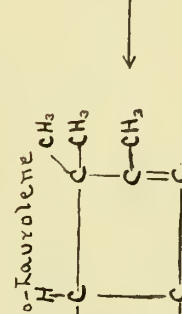
α-Campholytic Acid



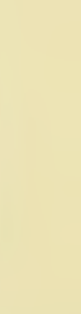
Hydro-Bromid of Campholytic Acid



Dihydro-Campholytic Acid



β-Campholytic Acid







## E X P E R I M E N T A L

Preparation of Camphoric Acid.<sup>1</sup>

In a four liter Jena flask with a test-tube condenser, water-cooled, were placed : -

225 g. of inactive camphor (Camphor Synthetisch-rein)

1800c.c. of nitric acid (sp.gr. 1.42)

1200c.c. of distilled water.

The flasks (duplicates were used) were placed on a steam bath and heated continuously for about seventy-two hours. The flasks were then allowed to cool. The crystals which separated out were camphoric acid. They were washed in water, dissolved in dilute ammonium hydroxide and reprecipitated with hydrochloric acid. After washing free from chlorine, the yield was 278 g.

The same two flasks with the mother liquors from which the camphoric crystals had been filtered off, were again placed upon the steam bath.

To each were added : -

225 g. of camphor

375 c.c. of nitric acid (sp.gr. 1.42)

These were again heated on the steam bath for seventy-two hours.

The yield after purifying in the same manner as before was 250 g.

- - - - -

1. Prof. Noyes; Am. Chem. J. 26, 501



Using the mother liquors from above for the third time

256 g. of camphor were added

600c.c. of nitric acid (sp.gr. 1.42)

The purified acid thus obtained was 518 g.

The mother liquors were then set aside for future use.

To determine whether the camphor used was active or inactive, a sample of the original was taken, dissolved in ethyl alcohol and tested by the polariscope. The mean reading of the alcoholic solution containing the camphor was the same as the mean reading of the alcoholic solution without the camphor. The sodium flame was used.

#### Preparation of Camphoric Anhydride.<sup>1</sup>

270 g. of camphoric acid.

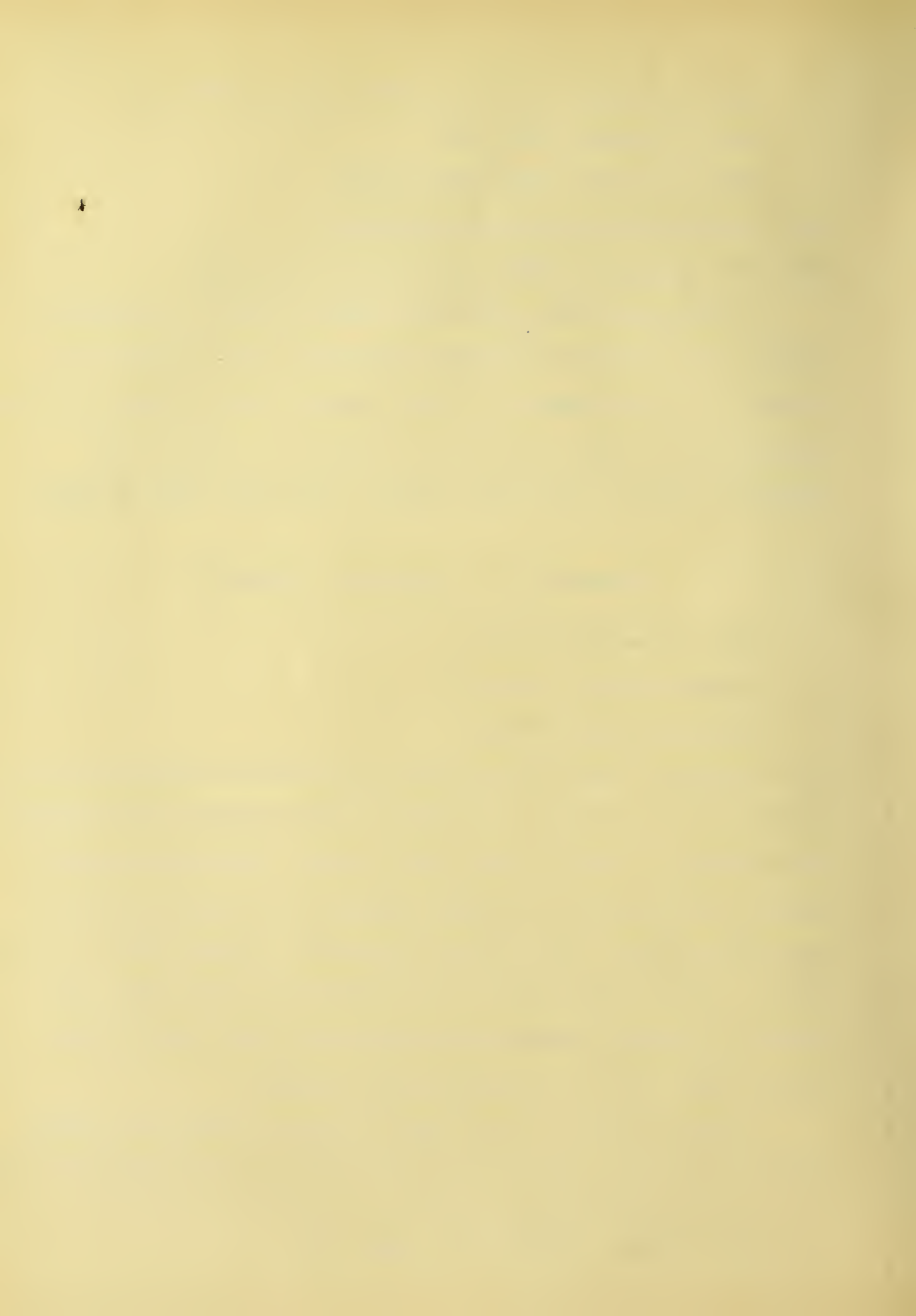
175c.c. of acetic anhydride

27c.c. of acetyl chloride.

were placed in a Jena flask, a water-cooled reflux condenser was used, and the mixture heated on the steam bath till the whole mass liquefied and was clear. This took about half an hour. The mixture was then allowed to cool and the anhydride extracted and recrystallised from hot ethyl alcohol. The yield when the acetic anhydride was good, was 215 g. At first the reaction did not take place, but after redistilling the acetic anhydride and taking that portion which boiled between  $138^{\circ}$  -  $140^{\circ}$ , good results were obtained.

It was found that it was better to warm the mixture in a long-necked flask over a low flame till the mixture was dissolved; to cool

1. Prof. Noyes; Am. Chem. J. 16, 502.



in a porcellain dish in the hood; to add about one hundred c.c. of water and to suck off sharply. Wash twice with water, recrystallise from alcohol, but avoid long warming with alcohol. This product may be washed twice with twenty c.c. of fifty per cent alcohol. The melting point was 1226°. If the action has gone correctly, a few crystals dissolved in alcohol to which a little phenolphthalein has been added, will give a permanent pink color with a single drop of tenth normal potassium hydroxide. The yield is from eighty to eighty-three per cent of the camphoric acid used.

#### Preparation of $\alpha$ and $\beta$ Camphoremidic Acids.<sup>1</sup>

In a pressure flask were placed,

100 g. of camphoric anhydride

100 c.c. of concentrated ammonium hydroxide.

The first time that the reaction was run, the bottle was placed in a steam bath and heated till the mixture cleared. But this did not seem to give as good results as when the flask was simply shaken in the air. The mixture usually cleared in about ten minutes. There was considerable action and quite a little heat was generated. Upon opening the flask, only a moderate pressure was observed but always a considerable odor of ammonia. The contents was poured into an open vessel and allowed to cool. After crystallisation had taken place, it was filtered on a porcellain funnel by suction.

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1. Prof. Noyes; Am. Chem. J. 16, 502





Both the  $\beta$  and  $\alpha$  acids are formed, but the ammonium salt of the  $\alpha$  acid is less soluble than that of the  $\beta$ . Therefore my first filtrate contained the  $\beta$  salt. This filtrate was treated with concentrated sodium hydroxide (1-3) but the sodium salt would not precipitate even upon inoculation, so the filtrate was treated with hydrochloric acid. This was added drop by drop with constant stirring so as to prevent if possible, the acid from coming down gummy. The  $\beta$  acid was filtered and dried by suction.

The crystals which were obtained at first, contained mostly the ammonium salt of the  $\alpha$  acid. This was treated with water. As small an amount of water was used as could be and still get all of the acid into solution that would go. The solution obtained in this way was treated with hydrochloric acid to precipitate the  $\alpha$  acid. The same caution was observed in this instance as with the  $\beta$  acid. This was filtered, and dried by suction.

### Preparation of Amino-Camphonanic Acid<sup>1</sup>

by

Hoffman's Reaction.

Two solutions were made up, viz = - I & III

Sol. I

35 g. of  $\alpha$ -camphoramidic acid.

175c.c. of sodium hydroxide (10%) cold.

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1. Am. Chem. J. 28, 483.

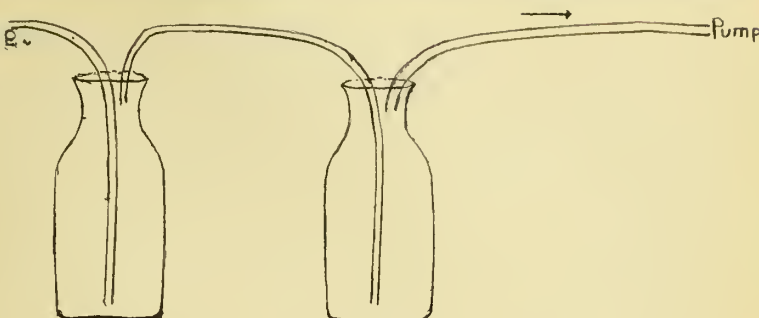


## Sol. III

8.9c.c. of bromine aspirated into

245c.c. of sodium hydroxide (10%) cold.

To make this last solution, two wash-bottles were used as shown in the accompanying drawing.



The second solution was added to the first and warmed for ten to fifteen minutes on the steam bath. The mixture was then cooled and to a small portion a little hydrochloric acid was added to see whether or not bromine was liberated. If so, sodium acid sulphate would have been added but not otherwise. No bromine appeared and to the whole mixture, ninety c.c. of concentrated hydrochloric acid were added. It was then evaporated to about one hundred and fifty c.c., filtered by suction, and to the filtrate thirty or forty c.c. of concentrated hydrochloric acid were added.

On cooling, the hydrochloride of the amino-camphonic acid crystallised. This was sucked off and the filtrate evaporated on the steam bath until the sodium chloride began to appear. To purify this chloride from some sodium chloride, we depend upon the difference in solubility. As is well known, sodium chloride is almost as soluble in cold water as it is in hot water, while the chloride of the amino-camphonic acid is much more soluble in hot water than it is in cold water. So by evaporating the filtrate until sodium chloride





began to appear, then filtering this off while the solution was hot, we got rid of the sodium chloride. Then by cooling the filtrate, the chloride of the amino-camphonic acid would crystallise out. The different crystals could be tested by ignition on a platinum foil to see whether they were organic or inorganic.

By recrystallising in water a product was obtained melting at  $265^{\circ}$ . This chloride upon standing in a dessicator, showed signs of having effloresced, so a small portion was taken and heated in a dry tube. Considerable moisture condensed on the upper portion of the tube. To find the exact amount, some of the chloride was allowed to crystallise from a water solution without chilling the solution. This was then dried between filter-papers. When a sample was placed in a porcelain crucible which had been brought to constant weight at  $100^{\circ}$  it was found to lose seven per cent at one hundred degrees. This chloride was heated in a water-jacketed air-bath; the temperature remaining from ninety eight to ninety nine and a half degrees. 0.1030 grams of the hydrochloride dried to constant weight at one hundred degrees centigrade, lost 0.0072 grams of water.

Calculated for  $C_{10}H_{17}O_3N$ ,  $HCl$ ,  $H_2O$

Theory = 7.01% of  $H_2O$

Found 7.2% " "



Hoffman's Reaction  
for the Preparation of the  
Dihydroaminocampholytic Acid.

In solution I 79.6 g. of  $\beta$ -camphoramidic acid was dissolved in  
400c.c. of sodium hydroxide solution (10%)

In solution II 20.4c.c. of bromine was aspirated into  
560c.c. of sodium hydroxide solution (10%)

The two solutions were mixed and then warmed on the steam bath  
for one half an hour. A small portion was tested with hydrochloric  
acid, to see if it contained an excess of bromine but none was found.

The mixed solutions were then poured into 132c.c. of concentrated  
hydrochloric acid and then more acid was added slowly till it gave a  
neutral spot-test to phenolphthalein. It was found that it must be  
kept neutral while evaporating or it became viscous and would not  
evaporate. An attempt was made to separate the sodium chloride out by  
fractional crystallisation but no good results were obtained. So after  
evaporating to dryness, a little more than the theoretical amount of  
hydrochloric acid was added to form the hydrochloride and the mixture  
was washed with absolute ethyl alcohol, as the hydrochloride is  
soluble in the alcohol. A little water was added to the extract in  
order to prevent the esterification while driving off the alcohol.

This residue was found to be not all soluble in water so it was  
washed thoroughly with cold water and crystallised. The same result  
was obtained but after once more washing and crystallising, then  
drying in vacuo, a clear solution was obtained when water was added.





The hydrochloride appears to be very soluble.

Decomposition of the Hydrochloride of  
Dihydroaminocampholytic Acid.

Twenty-two grams of the hydrochloride was dissolved in 50c.c. of water and placed in a 500c.c. round bottomed distilling flask. Eight grams of sodium nitrite were dissolved in 25c.c. of water and the two solutions cooled separately. With the aid of a pipette that reached to the bottom of the distilling-bulb, the sodium nitrite solution was placed underneath the hydrochloride solution. Action at once began and the temperature rose to fifty-three degrees.

Enough acid was obtained from the hydrochloride solution to form the nitrous acid from the nitrite. But after the action had pretty well ceased, a little dilute sulphuric acid (1:1) was added. The <sup>iso</sup>laurolene can be separated from this aqueous solution by distillation after the solution has been made alkaline with sodium hydroxide. All the <sup>iso</sup>laurolene will come over in the first thirty c.c. of the distillate. A little campholytic acid will be carried over also, but by making this distillate alkaline and redistilling, only the hydrocarbon and water will pass off. This was separated from the water and dried over calcium chloride. The boiling point was found to be from one hundred and eight to one hundred and nine degrees.

The residue from the distillate from which the hydrocarbon was obtained was added to the original solution; the whole acidified with





dilute sulphuric acid and repeatedly extracted with ether. Each extraction was washed with twenty c.c. of water to which had been added a little sodium sulphate ( each time using the same ether and washing with the same water ) This extract was dried by passing dry air through it.

This extract, which contains the hydroxy acid, campholytic acid, and the lactone was distilled with steam, the steam carrying with it the two latter. This distillate was extracted with ether and the residue was washed with potassium carbonate, thus forming the potassium salt of the campholytic acid. This solution was extracted with ether to obtain the lactone. The alkaline solution was made acid with hydrochloric acid and the precipitated campholytic acid extracted.

The residue containing the lactone was distilled with steam to purify it, extracted with ether and the residue treated with potassium permanganate to see if it contained the unsaturated campholytic acid. It was found to decolorize the solution and so was treated with sodium hydroxide (10%) care being taken not to form the hydroxy acid. When the lactone had been freed from the unsaturated acid it was extracted and dried with sodium sulphate and dried on the steam bath under diminished pressure. An attempt was made to crystallise the lactone and to obtain its melting point but it could not be crystallised.

The lactone obtained at this point was treated with two molecules of sodium hydroxide (10%) and heated on the water bath under reflux condenser for several hours. The hydroxy acid was precipitated with hydrochloric acid and after repeated crystallisation a constant melting point of  $116.3^{\circ}$  was obtained. This acid was titrated and a molecular weight of 169 was obtained. - Theoretical = 172



### The Hydrobromid of Campholytic Acid.

The campholytic acid obtained above was treated with hydrobromic acid, the latter being formed from the passing of hydrogen and bromine over heated platinumized asbestos. The campholytic acid was in a ligroin solution and the hydrobromid crystallised out as it was formed. A silver-bromide determination gave <sup>a result</sup> seven tenths of one ~~per~~ cent too high, which was probably due to the excess of the hydrobromic acid. The melting point of the hydrobromid was found to be eighty-three degrees but it was not sharp.

The hydrobromide was treated with about twice its weight of sodium bicarbonate; then aciduated, extracted with ether, and the residue distilled with steam. The campholytic acid and lactone were separated as stated above and the hydroxy acid formed from the lactone the same as before. The products gave the same melting points as on the first formation.





## CONCLUSION.

From the foregoing work it will be seen that the reactions in the inactive series so far as <sup>they</sup> have been tested, agree closely with the reactions in the active series. We did not find it practicable to separate the dihydroaminocampholytic acid from the salt which is formed by the Hoffman Reaction, by fractional crystallisation, so we prepared the hydrochloride and separated it by its solubility in absolute alcohol.

The campholytolactone has not been prepared before and we did not succeed in the present work in crystallising it. From this we prepared the hydroxy acid and its melting point agreed with the melting point of a mixture which Mr. L. E. Nickell prepared by mixing equal amounts of the dl-hydroxy acids

A new compound, the hydrobromid of campholytic acid, was prepared from campholytic acid, and to check our work we went back from this hydrobromid to the campholytic acid and the lactone. From the lactone we again prepared the hydroxy acid. This agrees with the reactions in the other series.









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